

10/722, 085

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NEWS 7 SEP 27 SWETSCAN will no longer be available on STN
NEWS 8 OCT 28 KOREAPAT now available on STN
NEWS 9 NOV 18 Current-awareness alerts, saved answer sets, and current
search transcripts to be affected by CERAB, COMPUAB, ELCOM,
and SOLIDSTATE reloads

NEWS EXPRESS OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004

NEWS HOURS STN Operating Hours Plus Help Desk Availability

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FILE 'HOME' ENTERED AT 17:51:13 ON 23 NOV 2004

=> file reg
COST IN U.S. DOLLARS

FULL ESTIMATED COST

| SINCE FILE
ENTRY | TOTAL
SESSION |
|---------------------|------------------|
| 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 17:51:23 ON 23 NOV 2004
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STRUCTURE FILE UPDATES: 22 NOV 2004 HIGHEST RN 786612-66-6
DICTIONARY FILE UPDATES: 22 NOV 2004 HIGHEST RN 786612-66-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

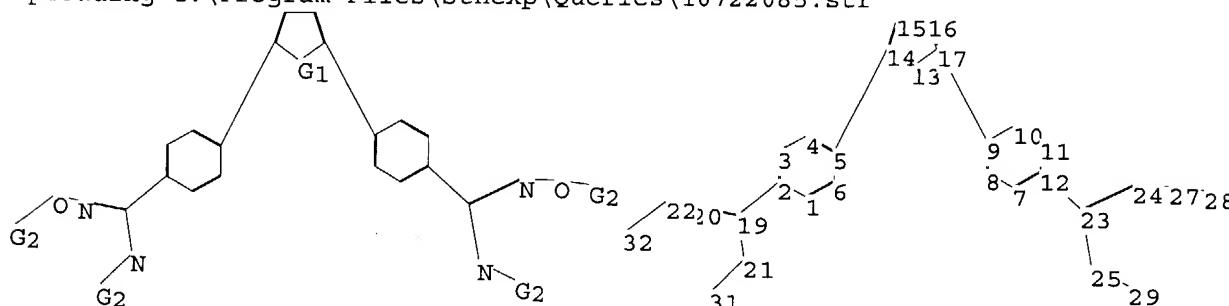
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10722085.str



chain nodes :

19 20 21 22 23 24 25 27 28 29 31 32

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17

chain bonds :

2-19 5-14 9-17 12-23 19-20 19-21 20-22 21-31 22-32 23-24 23-25 24-27
25-29 27-28

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-17
14-15 15-16 16-17

exact/norm bonds :

2-19 5-14 9-17 12-23 13-14 13-17 14-15 15-16 16-17 19-20 19-21 20-22
21-31 22-32 23-24 23-25 24-27 25-29 27-28

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12

G1:O,S,CH2,NH

G2:H,Cb,Ak

Match level :

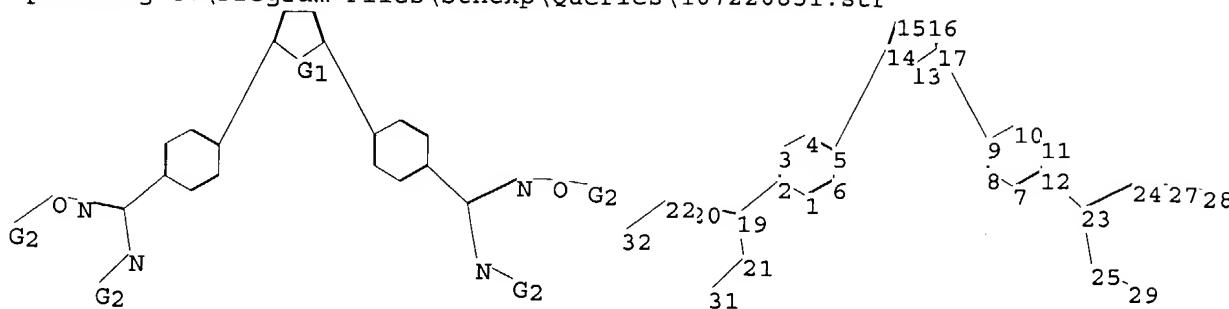
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11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 19:CLASS 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 27:CLASS 28:CLASS 29:CLASS
31:CLASS 32:CLASS

10/722,085

L1 STRUCTURE UPLOADED

=>

Uploading C:\Program Files\Stnexp\Queries\107220851.str



chain nodes :

19 20 21 22 23 24 25 27 28 29 31 32

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17

chain bonds :

2-19 5-14 9-17 12-23 19-20 19-21 20-22 21-31 22-32 23-24 23-25 24-27
25-29 27-28

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-17
14-15 15-16 16-17

exact/norm bonds :

2-19 5-14 9-17 12-23 13-14 13-17 14-15 15-16 16-17 19-20 19-21 20-22
21-31 22-32 23-24 23-25 24-27 25-29 27-28

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12

isolated ring systems :

containing 1 : 7 : 13 :

G1:O,S,CH2,NH

G2:H,Cb,Ak

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 19:CLASS 20:CLASS
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31:CLASS 32:CLASS

L2 STRUCTURE UPLOADED

=> S 12

SAMPLE SEARCH INITIATED 17:52:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 6 TO ITERATE

10/722,085

100.0% PROCESSED
SEARCH TIME: 00.00.01

6 ITERATIONS

0 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 6 TO 266
PROJECTED ANSWERS: 0 TO 0

L3 0 SEA SSS SAM L2

=> s 12 ful
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FULL SCREEN SEARCH COMPLETED - 131 TO ITERATE

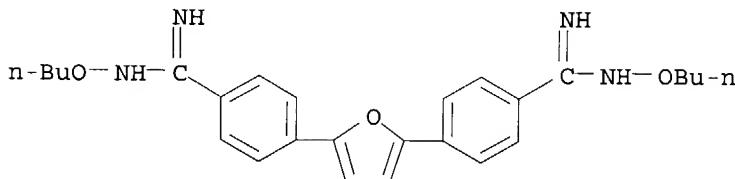
100.0% PROCESSED
SEARCH TIME: 00.00.01

131 ITERATIONS 18 ANSWERS

L4 18 SEA SSS FUL L2

=> d scan

L4 18 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Benzenecarboximidamide, 4,4'-(2,5-furandiy1)bis[N-butoxy- (9CI)
MF C26 H32 N4 O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus
COST IN U.S. DOLLARS
FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 156.26 | 156.47 |

FILE 'CAPLUS' ENTERED AT 17:53:15 ON 23 NOV 2004
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10/722,085

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FILE COVERS 1907 - 23 Nov 2004 VOL 141 ISS 22
FILE LAST UPDATED: 22 Nov 2004 (20041122/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s14
SL4 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s 14
L5      24 L4

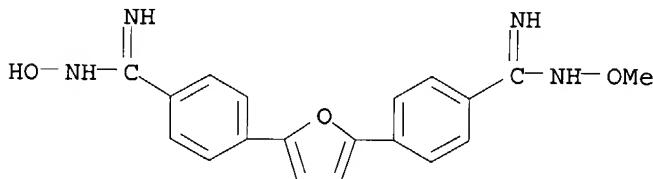
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    1337191 PROCESSES
    2994738 PROCESS
        (PROCESS OR PROCESSES)
    1408419 SYNTHES?
    199908 MAKE
    154085 MAKES
    344179 MAKE
        (MAKE OR MAKES)
    1122812 MADE
    24 MADES
    1122832 MADE
        (MADE OR MADES)
    1507696 PREPAR?
    113402 PREP
    2009 PREPS
    115210 PREP
        (PREP OR PREPS)
    1899226 PREPD
    21 PREPDS
    1899241 PREPD
        (PREPD OR PREPDS)
    104072 PREPG
    12 PREPGS
    104083 PREPG
        (PREPG OR PREPGS)
    2524098 PREPN
    197129 PREPNS
    2673564 PREPN
        (PREPN OR PREPNS)
    4431116 PREPAR?
        (PREPAR? OR PREP OR PREPD OR PREPG OR PREPN)
    237241 MAKING
    29 MAKINGS
    237264 MAKING
        (MAKING OR MAKINGS)
L6      16 L5 AND(PROCESS OR SYNTHES? OR MAKE OR MADE OR PREPAR? OR MAKING)

=> d 16 ibib hitstr abs 1-16

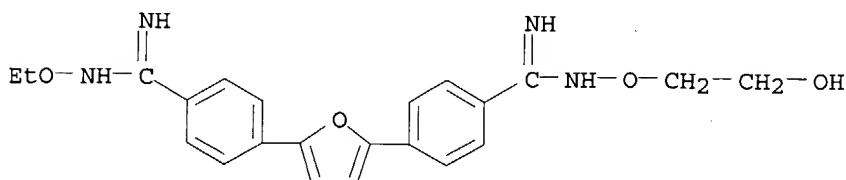
L6      ANSWER 1 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
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10/722,085

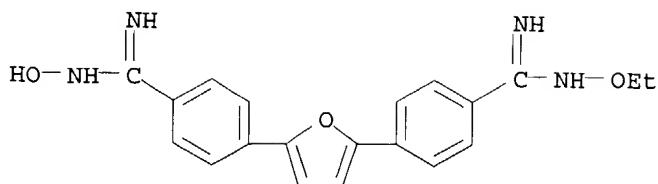
ACCESSION NUMBER: 2004:566930 CAPLUS
DOCUMENT NUMBER: 141:199478
TITLE: O-Alkoxyamidine Prodrugs of Furamidine: In Vitro Transport and Microsomal Metabolism as Indicators of in Vivo Efficacy in a Mouse Model of Trypanosoma brucei rhodesiense Infection
AUTHOR(S): Anseude, John H.; Anbazhagan, Mariappan; Brun, Reto; Easterbrook, Judy D.; Hall, James Edwin; Boykin, David W.
CORPORATE SOURCE: Division of Drug Delivery and Disposition School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599-7360, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(17), 4335-4338
PUBLISHER: CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: American Chemical Society
LANGUAGE: Journal English
IT 475976-08-0 743438-64-4 743438-66-6
743438-67-7 743438-68-8
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)
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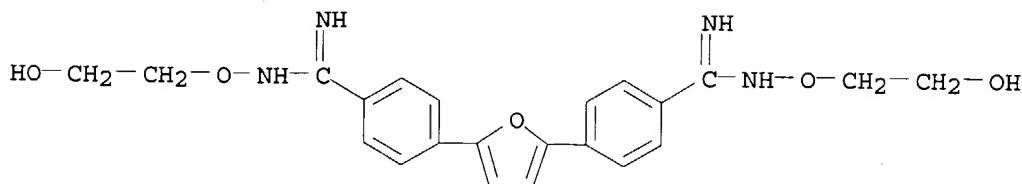
RN 743438-64-4 CAPLUS
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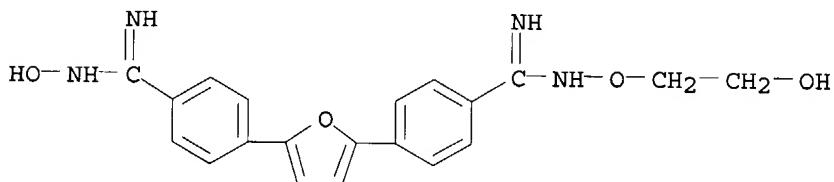
RN 743438-66-6 CAPLUS
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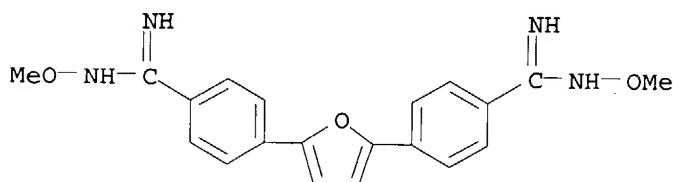
RN 743438-67-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(2-hydroxyethoxy)-] (9CI)
(CA INDEX NAME)



RN 743438-68-8 CAPLUS
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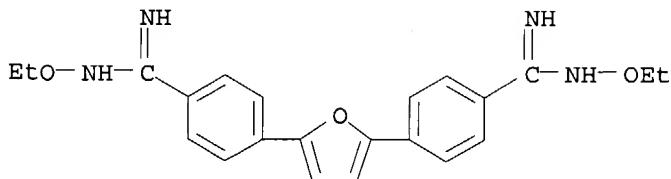
IT 186953-56-0P 186953-57-1P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)
RN 186953-56-0 CAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy-] (9CI) (CA INDEX NAME)



RN 186953-57-1 CAPLUS

10/722,085

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-ethoxy- (9CI) (CA INDEX NAME)



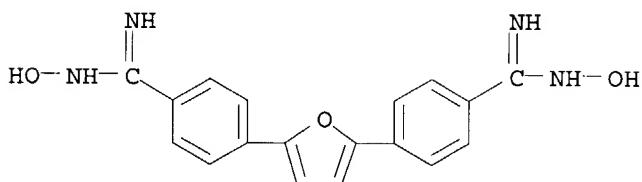
IT 186953-55-9P 582300-97-8P 743438-61-1P
743438-62-2P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)

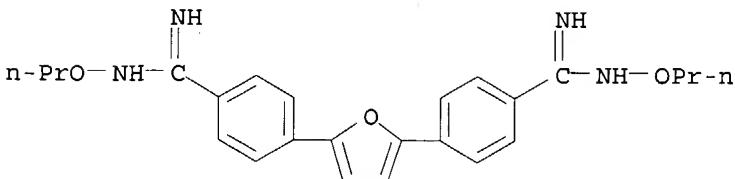
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CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



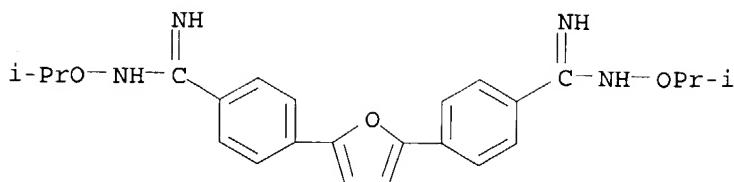
RN 582300-97-8 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-propoxy- (9CI) (CA INDEX NAME)

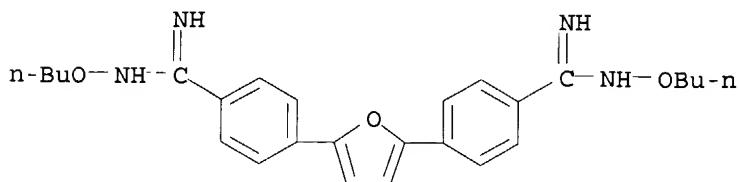


RN 743438-61-1 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethoxy)- (9CI) (CA INDEX NAME)



RN 743438-62-2 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(2,5-furandiyyl)bis[N-butoxy- (9CI) (CA INDEX NAME)]



AB Five O-alkoxyamidine analogs of the prodrug 2,5-bis[4-methoxyamidinophenyl]furan were **synthesized** and evaluated against Trypanosoma brucei rhodesiense in the STIB900 mouse model by oral administration. The observed in vivo activity of these prodrugs demonstrates that compds. with an O-methoxyamidine or O-ethoxyamidine group effectively cured all trypanosome-infected mice, whereas prodrugs with larger side-chains did not completely cure the mice. Permeability across Caco-2 cell monolayers and microsomal metabolism were used to identify the underlying mechanisms of prodrug efficacy.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2004:493958 CAPLUS
 DOCUMENT NUMBER: 141:54184
 TITLE: Cross-coupling **process** and palladium catalysts for the **synthesis** of bis-aryl diamidoxime compounds
 INVENTOR(S): Boykin, David W.; Anbazhagan, Mariappan; Tidwell, Richard R.
 PATENT ASSIGNEE(S): University of North Carolina at Chapel Hill, USA;
 Georgia State University Research Foundation, Inc.
 SOURCE: PCT Int. Appl., 16 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2004051217 | A2 | 20040617 | WO 2003-US37788 | 20031125 |
| WO 2004051217 | A3 | 20040708 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, | | | | |

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
 NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
 TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM,
 AZ, BY, KG, KZ

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
 BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
 MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
 GQ, GW, ML, MR, NE, SN, TD, TG

US 2004127721 A1 20040701 US 2003-722085 20031125

PRIORITY APPLN. INFO.: US 2002-429823P P 20021127

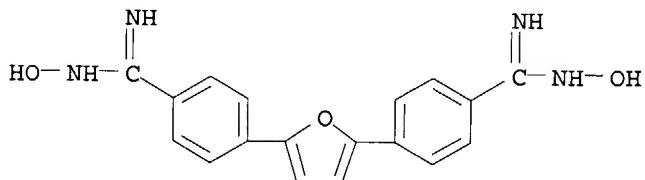
OTHER SOURCE(S): CASREACT 141:54184; MARPAT 141:54184

IT 186953-55-9P 186953-56-0P 186953-57-1P
 582300-97-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (cross-coupling process and palladium catalysts for the
 synthesis of bis-aryl diamidoxime compds.)

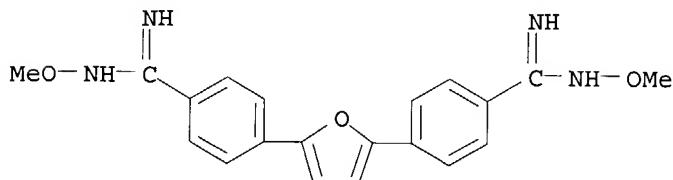
RN 186953-55-9 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



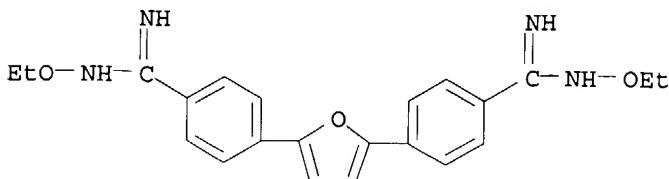
RN 186953-56-0 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



RN 186953-57-1 CAPLUS

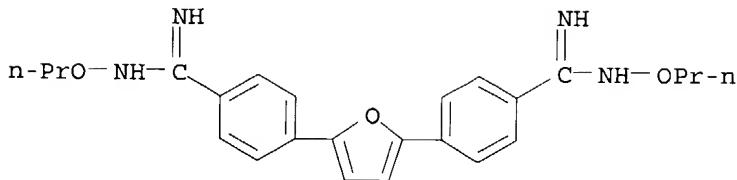
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-ethoxy- (9CI) (CA INDEX NAME)



RN 582300-97-8 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-propoxy- (9CI) (CA INDEX NAME)

INDEX NAME)



AB Bisaryl diamidoxime compds., such as 2,5-bis[4-hydroxy- and 4-O-alkylamidinophenyl]furans are prepared in high yield and selectivity from the one-step cross-coupling reaction of 2,5-bis(trialkylstannyl)heterocyclic compds. [e.g., 2,5-(bistributylstannyl)furan] with p-bromobenzamidoximes (e.g., p-bromobenzamidoxime) and their amidoxime ethers in the presence of a palladium catalyst [e.g., tetrakis(triphenylphosphine)palladium].

L6 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:991295 CAPLUS
 DOCUMENT NUMBER: 140:35966
 TITLE: Amidine derivatives for treating amyloidosis and neurodegenerative diseases
 INVENTOR(S): Chalifour, Robert J.; Kong, Xianqi; Wu, Xinfu; Lu, Wenshuo; Tidwell, Richard R.; Boykin, David
 PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA; Georgia State University Research Foundation, Inc.
 SOURCE: PCT Int. Appl., 92 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 2003103598 | A2 | 20031218 | WO 2003-US17992 | 20030609 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004147531 | A1 | 20040729 | US 2003-731463 | 20031205 |
| PRIORITY APPLN. INFO.: | | | US 2002-387001P | P 20020607 |
| | | | US 2001-316761P | P 20010831 |
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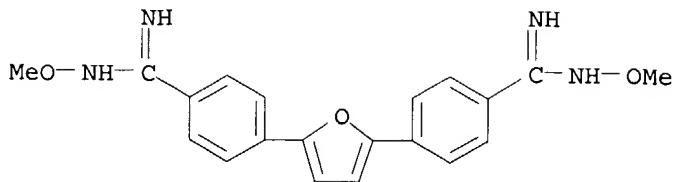
IT 186953-56-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of amidine derivs. for treating amyloidosis and neurodegenerative diseases)

RN 186953-56-0 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA)

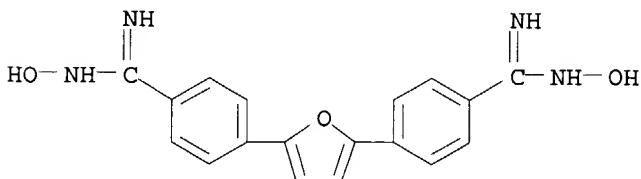
INDEX NAME)



AB The present invention relates to the use of amidine compds. in the treatment of amyloid related diseases. In particular, the invention relates to a method of treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amount of an amidine compound. Among the compds. for use according to the invention are those according to the following Formulas, such that, when administered, amyloid fibril formation, neurodegeneration, or cellular toxicity is reduced or inhibited.

L6 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:949264 CAPLUS
 DOCUMENT NUMBER: 140:93762
 TITLE: Direct conversion of amidoximes to amidines via transfer hydrogenation
 AUTHOR(S): Anbazhagan, Mariappan; Boykin, David W.; Stephens, Chad E.
 CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA
 SOURCE: Synthesis (2003), (16), 2467-2469
 CODEN: SYNTBF; ISSN: 0039-7881
 PUBLISHER: Georg Thieme Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 140:93762
IT 186953-55-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (conversion of amidoximes to amidines via transfer hydrogenation)
RN 186953-55-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



AB Amidoximes, O-alkylamidoximes, and O-acylamidoximes are directly converted to amidines by reaction with ammonium formate and Pd/C in HOAc.

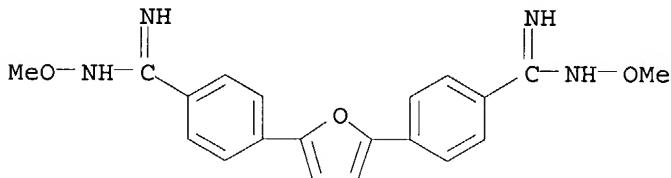
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:513253 CAPLUS

10/722,085

DOCUMENT NUMBER: 139:390750
TITLE: Detection of inhibition of bovine viral diarrhea virus by aromatic cationic molecules
AUTHOR(S): Givens, M. Daniel; Dykstra, Christine C.; Brock, Kenny V.; Stringfellow, David A.; Kumar, Arvind; Stephens, Chad E.; Goker, Hakan; Boykin, David W.
CORPORATE SOURCE: Department of Pathobiology, College of Veterinary Medicine, Auburn University, Auburn, AL, 36849, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2003), 47(7), 2223-2230
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:390750
IT 186953-56-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of bovine viral diarrhea virus by aromatic cationic mols.)
RN 186953-56-0 CAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



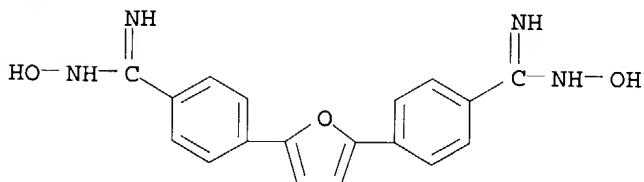
AB Bovine viral diarrhea virus (BVDV) is an economically significant pathogen of cattle and a problematic contaminant in the laboratory. BVDV is often used as an in vitro model for hepatitis C virus during drug discovery efforts. Aromatic dicationic mols. have exhibited inhibitory activity against several RNA viruses. Thus, the purpose of this research was to develop and apply a method for screening the aromatic cationic compds. for in vitro cytotoxicity and activity against a noncytopathic strain of BVDV. The screening method evaluated the concentration of BVDV in medium and cell lysates after 72 h of cell culture in the presence of either a 25 or 5 μ M concentration of the test compound. Five of 93 screened compds. were selected for further determination of inhibitory (90 and 50%) and cytotoxic (50 and 10%) concentration endpoints. The screening method identified compds. that exhibited inhibition of BVDV at nanomolar concns. while exhibiting no cytotoxicity at 25 μ M concns. The leading compds. require further investigation to determine their mechanism of action, in vivo activity, and specific activity against hepatitis C virus.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

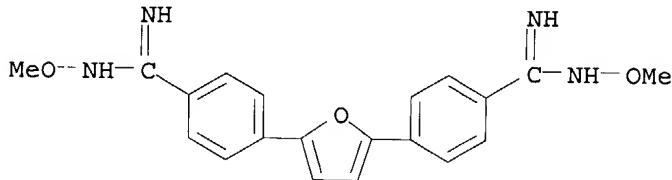
L6 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:416455 CAPLUS
DOCUMENT NUMBER: 139:197315
TITLE: A facile synthesis of the prodrug 2,5-bis(4-O-methoxyamidophenyl)furan and analogs

10/722,085

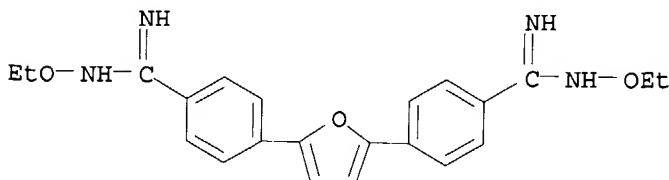
AUTHOR(S) : Anbazhagan, Mariappan; Boykin, David W.
CORPORATE SOURCE: Department of Chemistry, Georgia State University,
Atlanta, GA, 30303, USA
SOURCE: Heterocyclic Communications (2003), 9(2), 117-118
PUBLISHER: Freund Publishing House Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S) : CASREACT 139:197315
IT 186953-55-9P 186953-56-0P 186953-57-1P
582300-97-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 2,5-bis(4-O-methoxyamidinophenyl)furan and
analogs)
RN 186953-55-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA
INDEX NAME)



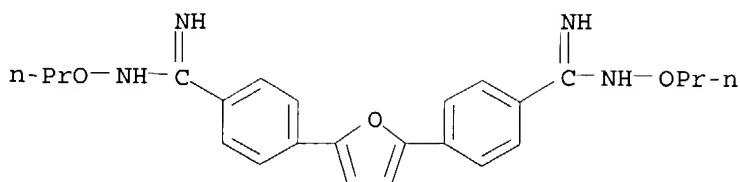
RN 186953-56-0 CAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA
INDEX NAME)



RN 186953-57-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-ethoxy- (9CI) (CA INDEX
NAME)



RN 582300-97-8 CAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-propoxy- (9CI) (CA
INDEX NAME)



AB A convenient **synthesis** of the prodrug 2,5-bis(4-O-methoxyamidinophenyl)furan and analogs using 2,5-bis(tri-n-butylstanny) furan and palladium catalyzed cross-coupling reactions is described. For example, refluxing 2,5-bis(tri-n-butylstanny) furan with O-propyl-p-bromobenzamidoxime in dioxane in the presence of tetrakis(triphenylphosphine)palladium for 16 h gave 70% 2,5-bis(4-O-propoxymimidinophenyl)furan.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:338839 CAPLUS

DOCUMENT NUMBER: 139:230527

TITLE: **Synthesis** of metabolites of the prodrug 2,5-bis(4-O-methoxyamidinophenyl)furan

AUTHOR(S): Anbazhagan, Mariappan; Saulter, Janelle Y.; Hall, James E.; Boykin, David W.

CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA

SOURCE: Heterocycles (2003), 60(5), 1133-1145
CODEN: HTCYAM; ISSN: 0385-5414

PUBLISHER: Japan Institute of Heterocyclic Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

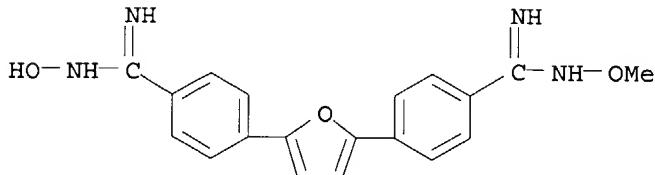
OTHER SOURCE(S): CASREACT 139:230527

IT 475976-08-0P, 4-[5-[4-[(Hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxybenzenecarboximidamide

RL: SPN (Synthetic preparation); PREP (Preparation)
(4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide] metabolite;
preparation of metabolites of prodrug [4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide]])

RN 475976-08-0 CAPLUS

CN Benzenecarboximidamide, 4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



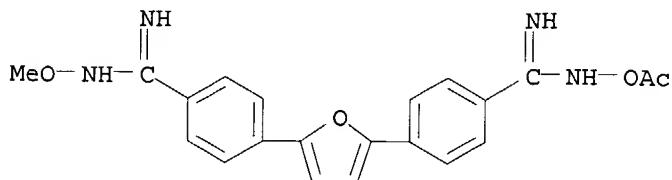
IT 591735-85-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

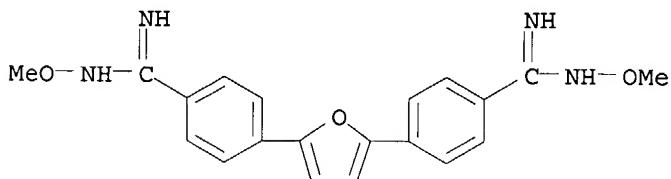
(preparation of metabolites of prodrug [4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide]])

10/722,085

RN 591735-85-2 CAPLUS
CN Benzenecarboximidamide, 4-[5-[4-[(acetyloxy)amino]iminomethyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



IT 186953-56-0DP, 4,4'-(2,5-Furandiyl)bis[N-methoxybenzenecarboximidamide], metabolites
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of metabolites of prodrug [4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide]])
RN 186953-56-0 CAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



AB The synthesis of three metabolites of the prodrug 2,5-bis(4-O-methoxyamidinophenyl)furan [i.e., 4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide]] was reported. Metabolites included 4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxybenzenecarboximidamide, 4-[5-[4-[(methoxyamino)iminomethyl]phenyl]-2-furanyl]benzenecarboximidamide and 4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]benzenecarboximidamide. The key step in each of the syntheses involves the Heck reaction.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:173414 CAPLUS
DOCUMENT NUMBER: 138:215350
TITLE: Amidine derivatives for treating amyloid-related diseases
INVENTOR(S): Chalifour, Robert J.; Kong, Xianqi; Wu, Xinfu; Lu, Wenshuo
PATENT ASSIGNEE(S): Neurochem Inc., Can.
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

| | | | | |
|---|--|----------|-----------------|-------------|
| WO 2003017994 | A1 | 20030306 | WO 2002-CA1353 | 20020903 ✓ |
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| US 2004006092 | A1 | 20040108 | US 2002-234643 | 20020903 |
| EP 1420773 | A1 | 20040526 | EP 2002-758012 | 20020903 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002012078 | A | 20040928 | BR 2002-12078 | 20020903 |
| US 2004147531 | A1 | 20040729 | US 2003-731463 | 20031205 |
| PRIORITY APPLN. INFO.: | | | US 2001-316761P | P 20010831 |
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| | | | US 2002-234643 | A1 20020903 |
| | | | WO 2002-CA1353 | W 20020903 |

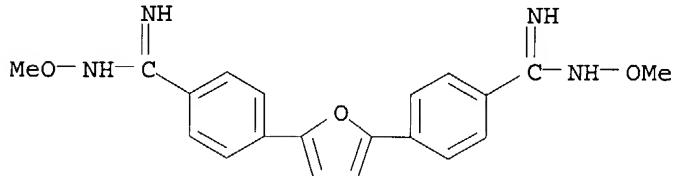
OTHER SOURCE(S) : MARPAT 138:215350

IT 186953-56-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (amidine derivs. for treating amyloid-related diseases)

RN 186953-56-0 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



AB The invention discloses the use of amidine compds. in the treatment of amyloid-related diseases (e.g. Alzheimer's disease, Down's syndrome, type II diabetes). In particular, the invention discloses a method for treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amount of an amidine compound. The compds. of the invention (Markush included) are such that, when administered, reduce or inhibit amyloid fibril formation, neurodegeneration, or cellular toxicity. Compound preparation is described.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:146280 CAPLUS

DOCUMENT NUMBER: 136:321920

TITLE: Antileishmanial activities of several classes of aromatic dications

AUTHOR(S): Brendle, James J.; Outlaw, Abram; Kumar, Arvind;

Boykin, David W.; Patrick, Donald A.; Tidwell, Richard R.; Werbovetz, Karl A.

CORPORATE SOURCE: Division of Experimental Therapeutics, Walter Reed Army Institute of Research, Silver Spring, MD, 20910, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2002), 46(3), 797-807

PUBLISHER: CODEN: AMACCQ; ISSN: 0066-4804
American Society for Microbiology

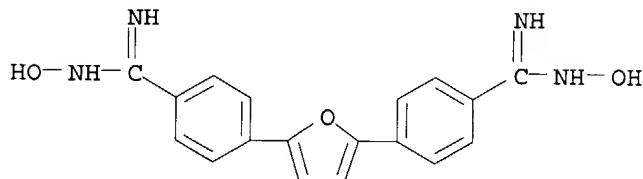
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 186953-55-9 186953-56-0

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antileishmanial activities of several classes of aromatic dications)

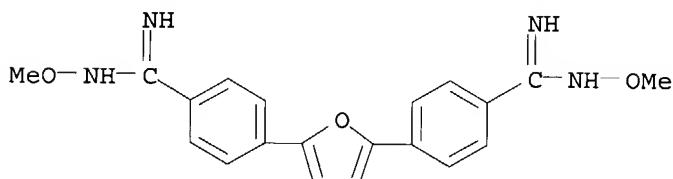
RN 186953-55-9 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)

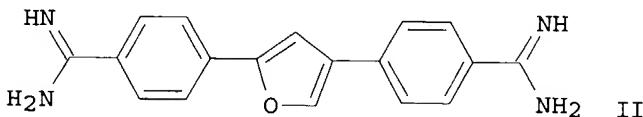
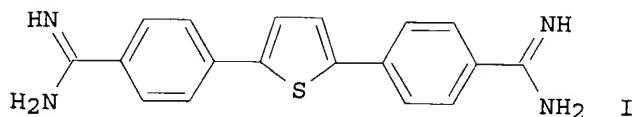


RN 186953-56-0 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



GI



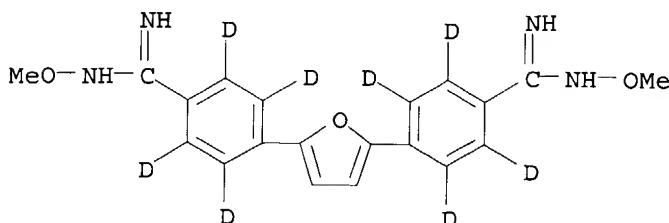
AB Aromatic dicationic mols. possess impressive activity against a broad spectrum of microbial pathogens, including *Pneumocystis carinii*,

Cryptosporidium parvum, and *Candida albicans*. In this work, 58 aromatic cations were examined for inhibitory activity against axenic amastigote-like *Leishmania donovani* parasites. In general, the most potent of the compds. were substituted di-Ph furan and thiophene dications.

2,5-Bis-(4-amidinophenyl)thiophene (I) was the most active compound. This agent displayed a 50% inhibitory concentration (IC₅₀) of $0.42 \pm 0.08 \mu\text{M}$ against *L. donovani* and an in vitro antileishmanial potency 6.2-fold greater than that of the clin. antileishmanial dication pentamidine and was 155-fold more toxic to the parasites than to a mouse macrophage cell line. 2,4-Bis-(4-amidinophenyl)furan (II) was twice as active as pentamidine (IC₅₀, $1.30 \pm 0.21 \mu\text{M}$), while 2,5-bis-(4-amidinophenyl)furan and pentamidine were essentially equipotent in our in vitro antileishmanial assay. Carbazoles, dibenzofurans, dibenzothiophenes, and benzimidazoles containing amidine or substituted amidine groups were generally less active than the di-Ph furans and thiophenes. In all cases, aromatic dications possessing strong antileishmanial activity were several-fold more toxic to the parasites than to a cultured mouse macrophage cell line. These structure-activity relationships demonstrate the potent antileishmanial activity of several aromatic dications and provide valuable information for the future design and synthesis of more potent antiparasitic agents.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2001:151106 CAPLUS
 DOCUMENT NUMBER: 134:326363
 TITLE: *Synthesis of deuterium-labeled 2,5-bis(4-amidinophenyl)furan, 2,5-bis[4-(methoxyamidino)phenyl]furan, and 2,7-diamidinocarbazole*
 AUTHOR(S): Stephens, Chad E.; Patrick, Donald A.; Chen, Heidi; Tidwell, Richard R.; Boykin, David W.
 CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA
 SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (2001), 44(3), 197-208
 PUBLISHER: John Wiley & Sons Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 134:326363
 IT 336786-82-4P 336786-93-7P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of deuterium-labeled bis(amidinophenyl)furan,
 bis[(methoxyamidino)phenyl]furan, and diamidinocarbazole)
 RN 336786-82-4 CAPLUS
 CN Benzene-2,3,5,6-d4-carboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy-(9CI) (CA INDEX NAME)



10/722,085

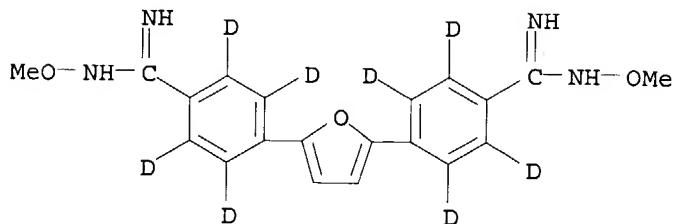
RN 336786-93-7 CAPLUS

CN Benzene-2,3,5,6-d4-carboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy-, (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 336786-82-4

CMF C20 H12 D8 N4 O3

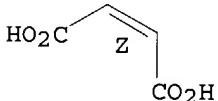


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



AB The **syntheses** of 2,5-bis(4-amidinophenyl)furan-d8 and 2,5-bis[4-(methoxyamidino)phenyl]furan-d8 from bromobenzene-d5 in six steps, and of 2,7-diamidinocarbazole-d6 from biphenyl-d10 in five steps, are described.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:50472 CAPLUS

DOCUMENT NUMBER: 134:120935

TITLE: Prodrugs for antimicrobial amidines

INVENTOR(S): Boykin, David W.; Rahmathullah, M. Syed; Tidwell, Richard R.; Hall, James E.

PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA

SOURCE: PCT Int. Appl., 45 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|-------|----------|-----------------|----------|
| ----- | ----- | ----- | ----- | ----- |
| WO 2001003685 | A2 | 20010118 | WO 2000-US18499 | 20000706 |
| WO 2001003685 | A3 | 20020711 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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 EP 1242059 A2 20020925 EP 2000-950293 20000706
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI,
 LT, LV, FI, RO, MK, CY, AL
 JP 2003504329 T2 20030204 JP 2001-508966 20000706
 US 6486200 B1 20021126 US 2000-612138 20000707
 US 2002019437 A1 20020214 US 2001-918787 20010731
 US 6503940 B2 20030107
 US 2003092755 A1 20030515 US 2002-208947 20020730
 US 6649652 B2 20031118
 PRIORITY APPLN. INFO.: US 1999-142826P P 19990708
 WO 2000-US18499 W 20000706
 US 2000-612138 A3 20000707
 US 2001-918787 B3 20010731

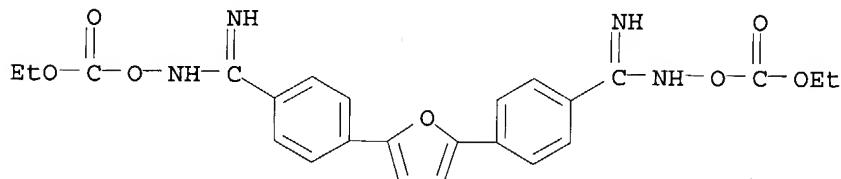
OTHER SOURCE(S) : MARPAT 134:120935

IT 247032-19-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prodrugs for antimicrobial amidines)

RN 247032-19-5 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[(ethoxycarbonyl)oxy] - (9CI) (CA INDEX NAME)

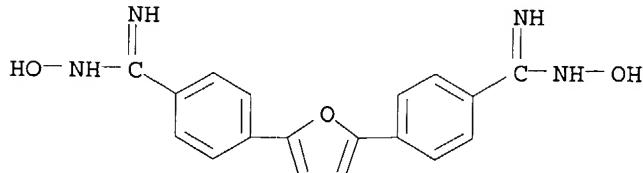


IT 186953-55-9P

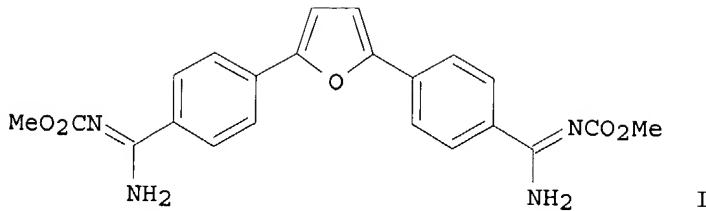
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prodrugs for antimicrobial amidines)

RN 186953-55-9 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



GI



AB A methods of treating an infection comprises administering a therapeutically effective amount of a bis(amidinophenyl)furan. E.g., I was prepared along with 10 other similar compds. and showed in vivo activity against *Pneumocystis carinii*.

L6 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:562085 CAPLUS

DOCUMENT NUMBER: 131:299327

TITLE: Prodrugs for Amidines: *Synthesis* and Anti-*Pneumocystis carinii* Activity of Carbamates of 2,5-Bis(4-amidinophenyl)furan

AUTHOR(S): Rahmathullah, Syed M.; Hall, James Edwin; Bender, Brendan C.; McCurdy, Donald R.; Tidwell, Richard R.; Boykin, David W.

CORPORATE SOURCE: Department of Chemistry and Center for Biotechnology and Drug Design, Georgia State University, Atlanta, GA, 30303, USA

SOURCE: Journal of Medicinal Chemistry (1999), 42(19), 3994-4000

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 131:299327

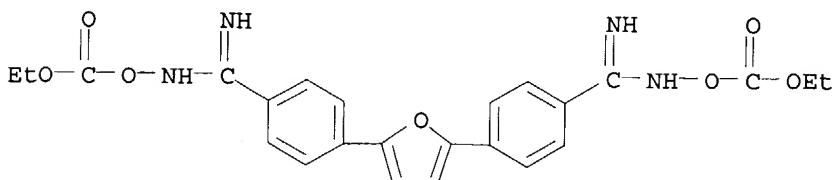
IT 247032-19-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and anti-*Pneumocystis carinii* activity of carbamates of bis(amidinophenyl)furan prepared from aryl alkyl and diaryl carbonates)

RN 247032-19-5 CAPLUS

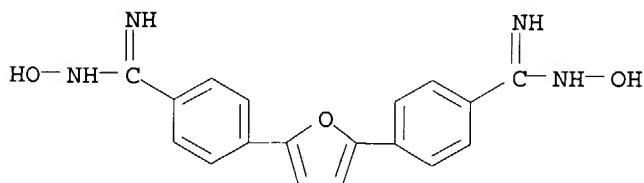
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[(ethoxycarbonyl)oxy] - (9CI) (CA INDEX NAME)



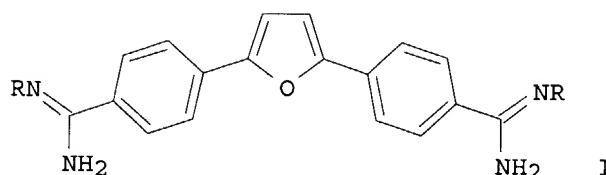
IT 186953-55-9

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation and anti-Pneumocystis carinii activity of carbamates
 of bis(amidinophenyl)furan prepared from aryl alkyl and diaryl
 carbonates)

RN 186953-55-9 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyil)bis[N-hydroxy- (9CI) (CA
INDEX NAME)

GI



I

AB **Syntheses** of several carbamate analogs of 2,5-bis(4-amidinophenyl)furan (I, R = H) under mild conditions and their evaluation as prodrugs against Pneumocystis carinii pneumonia (PCP) in an immunosuppressed rat model are described. Thus, nine new bis(carbamates) of bis(amidine) I [R = MeO₂C (II), Cl₃CCH₂O₂C (III), EtSCO (IV), PhCH₂O₂C (V), (4-methyl-2-oxo-1,3-dioxol-4-en-5-yl)methoxycarbonyl (VI), PhO₂C (VII), 4-FC₆H₄O₂C (VIII), 4-MeOC₆H₄O₂C (IX), AcOCHMeO₂C (X)] and a bis(carbonate) [R = EtOC(O)O (XI)] have been **synthesized** and evaluated. The *in vivo* results show that VIII and IX had the best anti-PCP activity by both i.v. and oral administration. Compds. III-VII were also more active than the parent drug I on oral administration. The acute toxicity usually exhibited by the parent amidine I at 22 µmol/kg/day on *i.v.* administration has been significantly reduced by the prodrug modifications, with the exception of compound X which exhibited some toxicity. The **syntheses** of several aryl alkyl and diaryl carbonates as efficient reagents for the **preparation** of carbamate derivs. from bis(aryl amidines) are also described.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:785675 CAPLUS

DOCUMENT NUMBER: 130:32999

TITLE: Benzamidoxime prodrugs as antipneumocystic agents

INVENTOR(S): Hall, James E.; Tidwell, Richard R.; Boykin, David W.

PATENT ASSIGNEE(S): Georgia State University Research Foundation Inc., USA; The University of North Carolina At Chapel Hill

SOURCE: U.S., 17 pp., Cont.-in-part of U.S. 5,723,495.
CODEN: USXXAM

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 5843980 | A | 19981201 | US 1996-751171 | 19961115 |
| US 5723495 | A | 19980303 | US 1995-558716 | 19951116 |
| CA 2237650 | AA | 19970522 | CA 1996-2237650 | 19961115 |
| US 6025398 | A | 20000215 | US 1998-127317 | 19980731 |
| US 6214883 | B1 | 20010410 | US 2000-477390 | 20000104 |
| AU 764937 | B2 | 20030904 | AU 2000-62473 | 20001004 |
| US 2001044468 | A1 | 20011122 | US 2001-759664 | 20010112 |
| US 6423737 | B2 | 20020723 | | |
| PRIORITY APPLN. INFO.: | | | US 1995-558716 | A2 19951116 |
| | | | AU 1997-11605 | A3 19961115 |
| | | | US 1996-751171 | A3 19961115 |
| | | | US 1998-127317 | A3 19980731 |
| | | | US 2000-477390 | A3 20000104 |

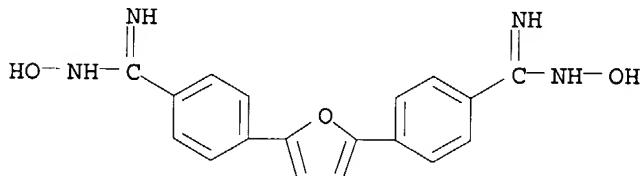
OTHER SOURCE(S): MARPAT 130:32999

IT 186953-55-9P 186953-56-0P 186953-57-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of benzamidoxime prodrugs as antipneumocystic agents)

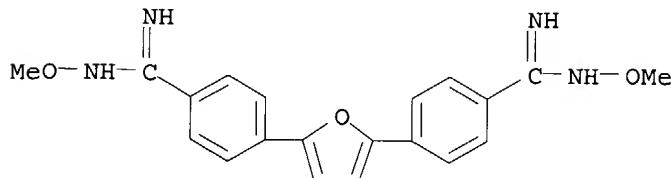
RN 186953-55-9 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



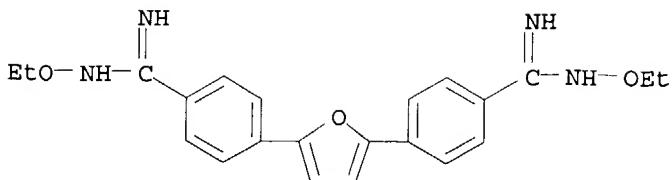
RN 186953-56-0 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)

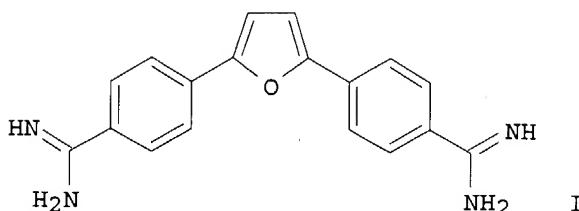


RN 186953-57-1 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-ethoxy- (9CI) (CA INDEX NAME)



GI



AB A method of treating *Pneumocystis carinii* pneumonia in a subject in need of such treatment is disclosed. The method comprises orally administering to the subject bis-benzamidoximes, such as I, which exhibited significant activity in infected rats (the anti-*Pneumocystis* value was expressed in percent of lung cysts in the treatment group vs. control group). The method of the present invention may alternatively comprise i.v. administering to the subject an active compound as disclosed herein. Pharmaceutical formulations and active compds. useful in the practice of the present invention are also disclosed.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:664986 CAPLUS

DOCUMENT NUMBER: 130:22621

TITLE: In vitro antifungal activities of a series of dication-substituted carbazoles, furans, and benzimidazoles

AUTHOR(S): Del Poeta, Maurizio; Schell, Wiley A.; Dykstra, Christine C.; Jones, Susan K.; Tidwell, Richard R.; Kumar, Arvind; Boykin, David W.; Perfect, John R.

CORPORATE SOURCE: Department of Medicine, Division of Infectious Diseases and International Health, Duke University Medical Center, Durham, NC, 27710, USA

SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(10), 2503-2510

PUBLISHER: CODEN: AMACQ; ISSN: 0066-4804
American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 186953-56-0

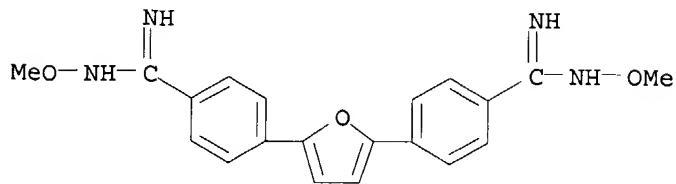
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(in vitro antifungal activities of a series of dication-substituted carbazoles, furans, and benzimidazoles)

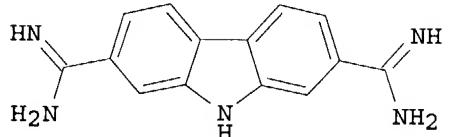
10/722,085

RN 186953-56-0 CAPLUS

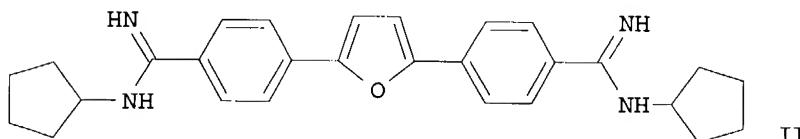
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



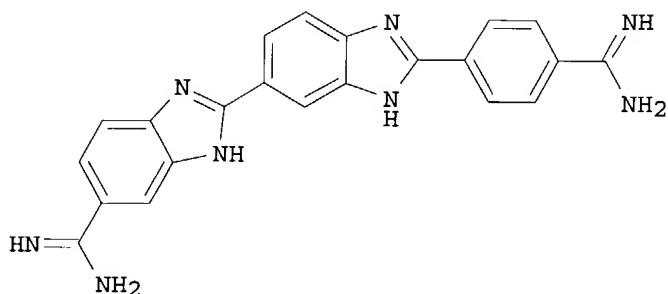
GI



I



II



III

AB Aromatic dicationic compds. possess antimicrobial activity against a wide range of eucaryotic pathogens, and in the present study an examination of the structures-functions of a series of compds. against fungi was performed. Sixty-seven dicationic mols. were screened for their inhibitory and fungicidal activities against *Candida albicans* and *Cryptococcus neoformans*. The MICs of a large number of compds. were comparable to those of the standard antifungal drugs amphotericin B and fluconazole. Unlike fluconazole, potent inhibitory compds. in this series were found to have excellent fungicidal activities. Broad-spectrum activities were observed for the carbazole I, the furan II, and the benzimidazole III. The MIC of III, one of the most potent compds., against *C. albicans* was 0.39 $\mu\text{g}/\text{mL}$, and it was the most potent compound against *C. neoformans* (MIC, $\leq 0.09 \mu\text{g}/\text{mL}$). Selected compds. were also found to be active against *Aspergillus fumigatus*, *Fusarium solani*, *Candida* species other than *C. albicans*, and fluconazole-resistant strains of *C. albicans* and *C.*

10/722,085

neoformans. Since of these compds. have been safely given to animals, these classes of mols. have the potential to be developed as antifungal agents.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:425344 CAPLUS
DOCUMENT NUMBER: 127:29074
TITLE: Benzamidoxime prodrugs as antipneumocystic agents.
INVENTOR(S): Hall, James Edwin; Tidwell, Richard Ray; Boykin, David Withers
PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA;
Georgia State University
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|-------------|
| WO 9717949 | A1 | 19970522 | WO 1996-US18496 | 19961115 |
| W: AU, CA, IL, JP, KR | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5723495 | A | 19980303 | US 1995-558716 | 19951116 |
| CA 2237650 | AA | 19970522 | CA 1996-2237650 | 19961115 |
| AU 9711605 | A1 | 19970605 | AU 1997-11605 | 19961115 |
| EP 861071 | A1 | 19980902 | EP 1996-942773 | 19961115 |
| R: CH, DE, ES, FR, GB, IT, LI | | | | |
| JP 2000500469 | T2 | 20000118 | JP 1997-519146 | 19961115 |
| AU 764937 | B2 | 20030904 | AU 2000-62473 | 20001004 |
| PRIORITY APPLN. INFO.: | | | US 1995-558716 | A 19951116 |
| | | | AU 1997-11605 | A3 19961115 |
| | | | WO 1996-US18496 | W 19961115 |

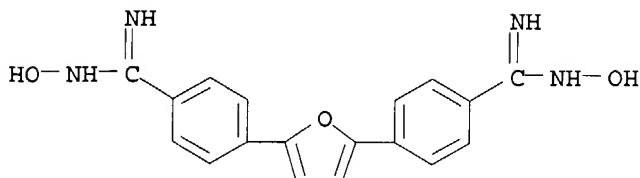
OTHER SOURCE(S): MARPAT 127:29074

IT 186953-55-9P 186953-56-0P 186953-57-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzamidoxime prodrugs as antipneumocystic agents.)

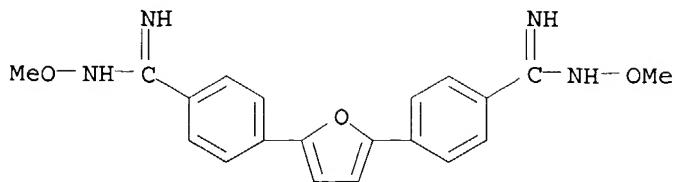
RN 186953-55-9 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)

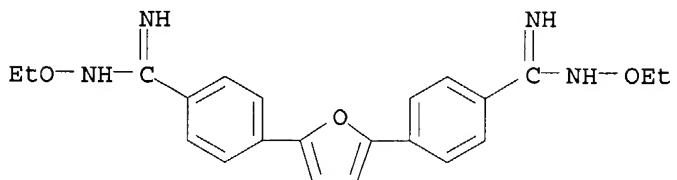


RN 186953-56-0 CAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)]



RN 186953-57-1 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-ethoxy- (9CI) (CA INDEX NAME)



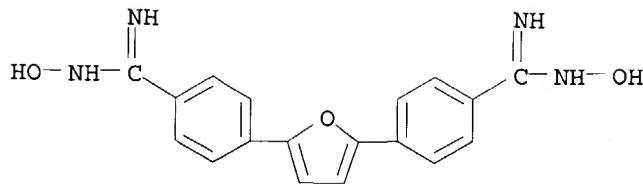
AB A method of treating *Pneumocystis carinii* pneumonia in a subject in need of such treatment is disclosed. The method comprises orally administering to the subject a bis-benzamidoxime, or a pharmaceutically acceptable salt thereof, that is reduced in the subject to produce a benzamidine having anti-*P. carinii* activity. The method of the present invention may alternatively comprise i.v. administering to the subject an active compound as disclosed herein. Pharmaceutical formulations and active compds. useful in the practice of the present invention are also disclosed. E.g., the compds. were **prepared** by reaction of 1,5-dibromopentane or 1,3-dibromopentane with the appropriate 4-hydroxybenzonitrile.

L6 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

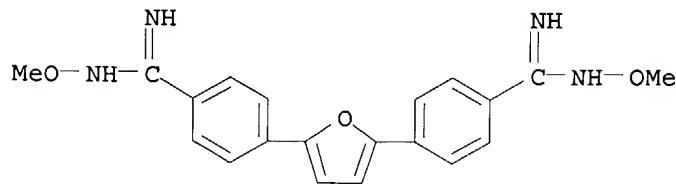
ACCESSION NUMBER: 1997:49577 CAPLUS
 DOCUMENT NUMBER: 126:152419
 TITLE: Anti-pneumocystis activity of bisamidoximes and bis-O-alkylamidoximes prodrugs
 AUTHOR(S): Boykin, David W.; Kumar, Arvind; Hall, James E.; Bender, Brendan C.; Tidwell, Richard R.
 CORPORATE SOURCE: Department Chemistry Center Biotechnology Drug Design, Georgia State University, Atlanta, GA, 30303, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(24), 3017-3020
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

IT 186953-55-9P 186953-56-0P 186953-57-1P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (anti-pneumocystis activity of bisamidoximes and bisalkylamidoximes prodrugs)

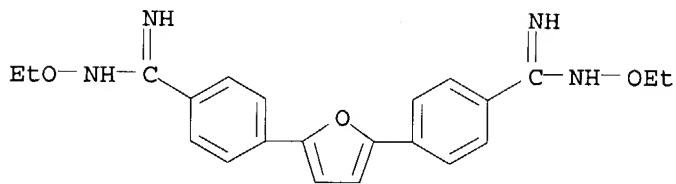
RN 186953-55-9 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



RN 186953-56-0 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)]



RN 186953-57-1 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-ethoxy- (9CI) (CA INDEX NAME)]



AB The authors report the **synthesis** of 2,5-bis-[4-amidinophenyl]furan bisamidoxime, the corresponding bis-O-methylamidoxime and bis-O-ethylamidoxime and their evaluation as prodrugs against *Pneumocystis carinii* pneumonia.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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